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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/655,915	09/05/2003	Alan D. Attie	960296.99080	8862

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EXAMINER	
SITTON, JEHANNE SOUAYA	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 02/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/655,915	ATTIE ET AL.	
	Examiner	Art Unit	
	Jehanne S. Sitton	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) *4-8* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: Notice to Comply

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group 1, claims 1-3, directed to SorCS1 in the reply filed on 12/7/2005 is acknowledged. The traversal is on the ground(s) that the subject matter of all groups, and particularly I, III, V, VII, and IX relating to the SorCS1 gene, gene products, and agents interacting therewith are inextricably linked, that applicant's do not believe that a search burden exists for searching all groups as the searches would overlap, and that a search of SorCS1 diagnostics and therapeutics would provide information regarding Groups I, III, V, VII, and IX. This is not found persuasive because the methods of group 1 are directed to determining the sequence of a gene or gene region while the methods of group III are directed to determining expression. These searches are not coextensive in scope as information regarding alleles of a gene would not, in many cases, be linked to expression of the gene. In the instant case, no allele affecting gene expression is taught by the specification. With regards to group V, protein expression is not necessarily correlated to RNA expression. With regard to groups VII and IX, art relating to SorCS1 alleles would be directed to genetic analysis methods of nucleic acids and would not provide any information regarding agents that act with SorCS1 protein or to possible therapeutic agents which would interact with a SorCS1 protein to treat type II diabetes. Accordingly, the searches are not only not coextensive, but the amount of overlap (SorCS1) is not sufficient to relieve the search burden in analyzing the claims for 102, 103, and 112 paragraph rejections. With regard to the arguments pertaining to groups commonly classified in the same class (435), or to the restriction between all of groups I-IX, it is noted that other groups are also directed to SorCS3, which is a structurally distinct gene from SorCS1, providing no

overlap, in most cases, for search. Accordingly, as the groups are patentably distinct, and a search burden exists for searching all or more than one of the groups, the restriction requirement is maintained. The requirement is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

2. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Specification

3. The disclosure is objected to because of the following: The specification teaches at page 5 that the human SorCS1 cDNA sequence and amino acid sequence are SEQ ID NOS 1 and 2, respectively. However a search of the sequences indicated that they correspond to SorCS3 cDNA and protein. Appropriate correction is required, however care should be taken not to enter new matter into the disclosure.

4. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the

reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Figure 2 lists a number of amino acid sequences which do not have a proper sequence identifier. See MPEP Chapter 2400. A substitute sequence listing in paper and computer readable form, is required, along with a statement that no new matter is added with the submission. Further, the specification should be amended in the Brief Description of the Drawings for Figure 2, to reflect the different SEQ ID NOS set forth in the Figure.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. There are many factors to be considered when determining whether there is sufficient evidence to support determination that a disclosure does not satisfy the enablement requirements and whether any necessary experimentation is undue. These factors have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples,

> (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The claims (claims 1-2) are drawn to a method of assessing whether a human subject is susceptible to type 2 diabetes by determining the allele in the genome of the subject of the SorCS1 gene or analyzing the nucleic acid sequence of the subject in the SorCS1 gene. Claim 3 is drawn to a method of determining if a human being is a candidate for developing type 2 diabetes by determining the sequence of the protein coding region of the SorCS1 gene, deducing the amino acid sequence encoded by the region sequenced, and comparing the amino acid sequence to SEQ ID NO: 4, wherein a difference indicates the human being is a candidate for developing type 2 diabetes.

The nature of the invention, therefore, requires the knowledge of predictive associations between any polymorphism or mutation in any region of the human SorCS1 gene and susceptibility to developing type 2 diabetes.

The claims recite "SorCS1" gene, however the specification provides no description of the SorCS1 *gene* from any source, including human. The specification teaches that SorCS1 *cDNA* and amino acid sequence are SEQ ID NOS 1 and 2 respectively, however a search of each sequence reveals that such are the sequence for SorCS3. Were SEQ ID NOS 1 to correspond to the SorCS1 cDNA, such disclosure does not provide a teaching of the full length SorCS1 gene, including introns, 5' and 3' untranslated regions, promoter, etc. With regard to Claim 3, the claim recites "protein coding region" of the SorCS1 gene, however it is known that in mice, different isoforms of SorCS1 exist. The specification does not teach whether the human SorCS1 protein has different isoforms, and if so, what the different isoforms of human SorCS1 are,

accordingly, it is not clear what "differences" with regard to SEQ ID NO "2" [or 4] would be indicative of susceptibility to type 2 diabetes, when different isoforms may exist for human SorCS1.

The specification teaches that the inventors began by narrowing the genetic region associated with severe type 2 diabetes to a 7 MB segment of mouse chromosome 19 (page 4, para 0017). The specification teaches that 2 genes previously found in the region were SorCS1 and SorCS3, which belong to a family sharing a large region of similarity including the VPS10 domain. The specification teaches that due to similarity with sortilin, SorCS1 and SorCS3 are expected to be involved in insulin-stimulated glucose transportation and in controlling body fat metabolism. The specification teaches that the 7MB region was characterized and that it was found that the only difference between severely diabetic mice and less severely affected mice was 3 mutations in SorCS1, leading to 3 amino acid changes (table 1). The specification, however, does not teach the specific function or activity of SorCS1. The specification does not teach if other mutations occurred in other portions of the mouse genome that may be responsible for the severe form of diabetes observed in the mice.

The specification provides no teaching or working examples of any mutations in any portion of the SorCS1 gene in humans, or an association between SorCS1 alleles in a human subject and type II diabetes susceptibility. The specification asserts at page 3 that the SorCS1 gene in mice is "directly analogous" to the human gene, however this statement is unclear. The genes are not identical, and the meaning of "directly analogous" cannot be determined. For example, at table 1, the specification teaches different mutations at specific positions of mouse SorCS1. The specification teaches a mutation at position 50 from Thr to Ile, at position 1139

from Ser to Phe, and at position 1149 from Ser to Pro. In humans, however, position 50 is Alanine, position 1139 is Glycine, and position 1149 (in SEQ ID NOS 4) is Arginine. None of these amino acids are "directly analogous" to either amino acid found in mice at each position. The specification provides no teaching of the specific function or activity for SorCS1, or any of these 3 positions, accordingly the affect of each amino acid at such positions is unpredictable. Therefore, given the lack of guidance from the specification as to any mutations in any region of the SorCS1 gene in humans, a teaching of the function or SorCS1 including critical amino acids and domains required for function, or a predictable correlation between the presence of SorCS1 mutations and diabetes susceptibility in other species, the skilled artisan would be unable to predict an association between any mutation in any portion of the SorCS1 gene in humans and susceptibility to type 2 diabetes.

The specification's assertions with regard to putative SorCS1 activity is based on homology analysis with sortilin and the family of proteins that contains a VPS10 domain (page 4, end of para 00017). However, it is known for nucleic acids as well as proteins that even a single nucleotide or amino acid change or mutation can destroy or alter the function of a biomolecule in many instances, albeit not in all cases. The effect of these changes are largely unpredictable as to which ones have a significant effect verses not. The prior art does not teach the function of SorCS1 or how it is involved in type 2 diabetes. The post filing specifically date art provides some characterization of SorCS1 (see Hermey et al, JBC, vol. 278, Feb. 2003, pages 7390-7396), but teaches that neither the mature luminal domain nor any of the cytoplasmic domains of the different SorCS1 isoforms bound any of the ligands previously shown to interact with sortilin and SorLA, demonstrating sorCS1 is functionally different from the previously characterized Vps10-D family receptors (para bridging pages 7390-7391).

Additionally, Hermey teaches that the different isoforms of SorCS1 have completely different cytoplasmic domains that mediate different trafficking in cells (abstract). It is clear that the art supports that SorCS1 has a different function than other Vps10 domain family members, and that the 3 different isoforms of SorCS1 do not function in the same manner where the different cytoplasmic domain for each isoform mediates different trafficking in cells.

The instant specification provides no teaching or guidance as to the role of critical amino acids in any of the isoforms of either murine or human SorCS1 nor how such are involved in susceptibility to type 2 diabetes. The specification provides no predictable association that any alteration, in any region of the SorCS1 gene, in humans, let alone any species, is diagnostic or indicates a susceptibility for developing type 2 diabetes. No common element or attributes of the sequences are disclosed which would permit selection of sequences as polymorphisms. No structural limitations or requirements which provide guidance on the identification of sequences which meet these functional limitations of associating a polymorphism with type 2 diabetes is provided. Further, these claims expressly encompass allelic variants including insertions, deletions, substitutions and transversions at thousands of different sites. No written description of alleles, of upstream or downstream regions containing additional sequence, which are associated with any phenotype are described in the specification. No predictable correlation between the structural alterations in the mouse sequence and susceptibility for developing type 2 diabetes has been taught by the specification. Additionally, the specification provides no evidence that any SNP or mutation at such position in humans provides a predictable association with type 2 diabetes. The polymorphisms shown are not representative of the genus of any polymorphism associated with type 2 diabetes because it is not clear which polymorphisms

within the SorCS1 gene would have the same affect. The specification does not teach the function of SorCS1 nor how it's function, or lack of function, or altered function are predictably associated with type 2 diabetes.

The quantity of experimentation in this area is extremely large as it requires analysis of each position in the SorCS1 gene, which has not been taught by the specification or the art, to determine whether any alteration at each position is associated with type 2 diabetes. As neither the art nor the specification provide guidance as to which alterations at positions throughout SorCS1 are associated with type 2 diabetes, such analysis is replete with trial and error experimentation, with the outcome of each analysis being unpredictable. Screening each possible alteration in the SorCS1 gene represents an inventive and unpredictable undertaking in itself, with each of the many intervening steps, not providing any guarantee of success.

In order to practice the invention as claimed, one would first have to establish that a predictive relationship exists between mutations in any region of the SorCS1 gene and type 2 diabetes in humans. Further, the scope the claims requires knowledge of an association between all mutations in SorCS1 and type 2 diabetes. Due to the scope of the claims, one would be required to further undertake extensive trial and error experimentation with a large number of patients to determine mutations that share a predictive increased susceptibility of type 2 diabetes.

Thus, given the broad claims in an art whose nature is identified as unpredictable, the state of the prior art, the lack of guidance in the specification, the breadth of the claims and the quantity of experimentation necessary to practice the claimed invention, it would require undue experimentation to practice the invention commensurate in scope with the claims.

7. Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims (claims 1-2) are drawn to a method of assessing whether a human subject is susceptible to type 2 diabetes by determining the allele in the genome of the subject or analyzing the nucleic acid sequence of the subject in the SorCS1 gene. Claim 3 is drawn to a method of determining if a human being is a candidate for developing type 2 diabetes by determining the sequence of the protein coding region of the SorCS1 gene, deducing the amino acid sequence encoded by the region sequenced, and comparing the amino acid sequence to SEQ ID NO: 4, wherein a difference indicates the human being is a candidate for developing type 2 diabetes.

The claims recite "SorCS1" gene, however the specification provides no description of any SorCS1 *gene* from any source, including human. The specification teaches that SorCS1 cDNA and amino acid sequence are SEQ ID NOS 1 and 2 respectively, however a search of each sequence reveals that such are the sequence for SorCS3 . Additionally, the claims recite "protein coding region" of the SorCS1 gene, however it is known that in mice, different isoforms of SorCS1 exist. The specification does not teach the different isoforms of human SorCS1, accordingly, it is not clear what "differences" with regard to SEQ ID NO 2 [or 4] would be indicative of susceptibility to type 2 diabetes, when different isoforms may exist for human SorCS1.

The specification provides no teaching or working examples of any mutations in any portion of the SorCS1 gene in humans, or an association between SorCS1 alleles in a human subject and type II diabetes susceptibility. The specification asserts at page 3 that the SorCS1 gene in mice is "directly analogous" to the human gene, however this statement is unclear. The genes are not identical, and the meaning of "directly analogous" cannot be determined. For example, at table 1, the specification teaches that different mutations at specific positions of mouse SorCS1. The specification teaches a mutation at position 50 from Thr to Ile, at position 1139 from Ser to Phe, and at position 1149 from Ser to Pro. In humans, however, position 50 is Alanine, position 1139 is Glycine, and position 1149 (in SEQ ID NOS 4) is Arginine. None of these amino acids are "directly analogous" to either amino acid found in mice at each position. The specification provides no teaching of the specific function or activity for SorCS1, or any of these 3 positions, accordingly the affect of each amino acid at such positions is unknown. Further, the post filing specifically date art provides some characterization of SorCS1 (see Hermey et al, JBC, vol. 278, Feb. 2003, pages 7390-7396), but teaches that neither the mature luminal domain nor any of the cytoplasmic domains of the different SorCS1 isoforms bound any of the ligands previously shown to interact with sortilin and SorLA, demonstrating sorCS1 is functionally different from the previously characterized Vps10-D family receptors (para bridging pages 7390-7391). It is clear from the teachings of the post filing date art that different isoforms of SorCS1 exist, for which the specification provides no description.

The specification provides no predictable association that any alteration, in any region of the SorCS1 gene, in humans, let alone any species, is diagnostic or indicates a susceptibility for developing type 2 diabetes. No common element or attributes of the sequences are disclosed

which would permit selection of sequences as polymorphisms. No structural limitations or requirements which provide guidance on the identification of sequences which meet these functional limitations of associating a polymorphism with type 2 diabetes is provided. Further, these claims expressly encompass allelic variants including insertions, deletions, substitutions and transversions at thousands of different sites. No written description of alleles, of upstream or downstream regions containing additional sequence, which are associated with any phenotype are described in the specification. No predictable correlation between the structural alterations in the mouse sequence and susceptibility for developing type 2 diabetes has been taught by the specification. Additionally, the specification provides no evidence that any SNP or mutation at such position in humans provides a predictable association with type 2 diabetes. The polymorphisms shown are not representative of the genus of any polymorphism associated with type 2 diabetes because it is not clear which polymorphisms within the SorCS1 gene would have the same affect. The specification does not teach the function of SorCS1 nor how it's function, or lack of function, or altered function are predictably associated with type 2 diabetes.

In analysis of the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note regarding genus/species situations that "Satisfactory disclosure of a ``representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.) In the instant case, the specification fails to teach the necessary common attributes or features of the genus of encompassed nucleic acids (different

isoforms not taught) and polymorphisms in view of the species disclosed. As such, one of skill in the art would not recognize that applicant was in possession of the genus of nucleic acids and polymorphisms or mutations encompassed by the broadly claimed invention.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

The skilled artisan cannot envision the detailed chemical structure of the encompassed nucleic acids and polymorphisms, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993), and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. The current situation is a definition of the compound solely based on its functional utility, as a polymorphism, without any definition of the particular polymorphisms claimed.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it

obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

Conclusion

8. No claims are allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Sitton whose telephone number is (571) 272-0752. The examiner can normally be reached Monday-Thursday from 8:00 AM to 5:00 PM and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272-0745. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Jehanne Sitton

Jehanne Sitton
Primary Examiner
Art Unit 1634
2/6/06

Notice to Comply	Application No.	Applicant(s)
	10/655,915	ATTIE et AL.
	Examiner	Art Unit
	Jehanne Sitton	1634

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set in the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☐ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☒ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☐ 7. Other:

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", **as well as an amendment specifically directing its entry into the application.**

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (571) 272-2510
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